Remarks

Applicants have amended claims 88, 96, 104, 112, 114-123, 125, 133, 135-144, 146, 154, 157, 165, 174, and 182. Attached hereto is a marked-up version of the changes made by the current amendments, captioned "Version With Markings To Show Changes Made." The amendments are fully supported by the specification and claims as originally filed, and thus no new matter has been added.

Claims 76-182 are pending. Applicants respectfully request that the Examiner consider the above amendments and following remarks.

I. Rejections Under 35 U.S.C. §§ 101 and 112, First Paragraph

The Examiner has rejected claims 76-182 under 35 U.S.C. § 101 because the invention is allegedly not supported by either a specific and substantial asserted utility or a well established utility. *See* Paper No. 27, pages 2-4 and 8-10. In particular, the Examiner maintained the prior rejection on the basis that the assertion in the specification that t-PALP is useful for the same therapeutic uses as t-PA was not credible. The Examiner argues that:

> [t]here is no evidence of record or any line of reasoning that would support a conclusion that the t-PALP of the instant application was, as of the filing date, useful for the same purposes as t-PA.
>
> Paper No. 27, page 9.

The Examiner also rejected claims 166-182 under 35 U.S.C. § 101, asserting that "the instant specification does not disclose a credible 'real world' use for a DNA comprising 30/50 nucleotides." Paper No. 27, page 4.

The Examiner further rejected claims 76-182 under 35 U.S.C. § 112, first paragraph, because one skilled in the art would allegedly not know how to use the claimed

invention because it is supposedly not supported by either an asserted utility or a well established utility.

Applicants respectfully disagree and traverse the instant rejection.

Preliminarily, Applicants again point out that the specification asserts utilities for t-PALP, including: (1) treating vascular disease, such as stroke, deep-vein thrombosis, peripheral arterial occlusion, pulmonary embolism, and myocardiothrombosis, and (2) induction of growth of hepatocytes and regeneration of liver tissue. *See, e.g.*, page 6, line 23 to page 7, line 1. Applicants note that the Examiner does not appear to question the specificity or the substantiality of these asserted utilities for t-PALP, but instead questions their credibility. However, "an applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. 101." M.P.E.P. § 2107.02(III)(A) at 2100-39; *see also In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA 1974). Thus, the Examiner's assertion that "a protein of SEQ ID NO:2 is deemed to be an uncharacterized protein that needs further characterization" is improper under the Utility Guidelines, as Applicants have already attributed a utility in the specification for t-PALP that is presumptively sufficient. Rather, the burden is on the Examiner to establish that it is more likely than not that a person of ordinary skill in the art would not consider the utility asserted by Applicants to be specific, substantial, and credible. *See* M.P.E.P. § 2107 at 2100-30.

Such a *prima facie* showing must contain (1) an explanation that clearly sets forth the reasoning used in concluding that the asserted utility for the claimed invention is not specific, substantial, and credible; (2) support for factual findings relied upon in reaching this conclusion; and (3) an evaluation of all relevant evidence of record, including utilities taught in the closest prior art. *See id.* Moreover, the Examiner must establish why it is

more likely than not that one of ordinary skill in the art would doubt *(i.e.,* "question") the truth of the statement of utility. *See id.*; *see also In re Brana,* 51 F.3d 1560, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995). For the reasons set forth below, Applicants maintain that the Examiner has not met this burden.

Although the Examiner has not questioned the specificity or substantiality of the asserted utilities, the asserted utilities for t-PALP are in fact specific (*e.g.*, not every protein may be employed for treating vascular disease) and substantial ("the general rule [is] that the treatments of specific diseases or conditions meet the criteria of 35 U.S.C. § 101." (Revised Interim Utility Guidelines Training Materials, p. 6)). Indeed, Applicants respectfully point out that the USPTO's discussion of therapeutic proteins at pages 27-29 of the Revised Interim Utility Guidelines Training Materials makes clear that the above disclosed utilities are specific and substantial under the Guidelines.

With respect to credibility, in the instant rejection, the Examiner bases the allegation that the asserted utility is not credible on: (1) the degree of homology between t-PALP and t-PA; and (2) the absence of "evidence of an enzymatic activity" for t-PALP in the specification. Thus, the Examiner asserts that absent a higher degree of homology between t-PA and t-PALP, or experimental proof of t-PALP's enzymatic activity, the asserted utilities lack credibility. However, as discussed above, Applicants' asserted utilities are presumptively credible under the Utility Guidelines, absent a showing by the Examiner that a person of ordinary skill in the art would more likely than not consider such utilities not credible. Applicants submit that the Examiner has presented no evidence to disprove or even contradict the utilities asserted in the specification for t-PALP. For example, the Examiner has not alleged that the known uses of t-PA are inconsistent with the asserted utilities for t-PALP. Further, Applicants note that the burden is not on

Applicants to prove the activity of the protein, it is on the Examiner to establish that Applicants' asserted utility is not credible. Applicants respectfully maintain that the Examiner has not met this burden.

Indeed, there is no need to prove that a correlation exists between a particular activity and an asserted diagnostic or therapeutic use of a compound as a matter of statistical certainty or provide actual evidence of success in treating humans where such a utility is asserted. M.P.E.P. §§ 2107.01 to 2107.03. Moreover, "[u]sefulness in patent law, and in particular in the context of pharmaceutical inventions, *necessarily* includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans." *In re Brana,* 51 F.3d 1560, 1568 (Fed. Cir. 1995) (emphasis added).

Thus, in view of the above, Applicants respectfully submit that the presently claimed invention possesses specific, substantial, and credible utilities which constitute patentable utilities under 35 U.S.C. § 101. Because Applicants' assertions of utility are sufficient to satisfy the requirements of 35 U.S.C. § 101, it is respectfully requested that the Examiner's rejection of the claims under 35 U.S.C. § 101 be reconsidered and withdrawn.

Further, the Federal Circuit and its predecessor determined that the utility requirement of 35 U.S.C. § 101 and the how to use requirement of 35 U.S.C. § 112, first paragraph, have the same basis, *i.e.*, the disclosure of a credible utility. *See In re Brana*, 51 F.3d 1560, 1564, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995); *see also* M.P.E.P. § 2107(IV); Utility Examination Guidelines at 1098. As discussed above, the specification teaches specific, substantial, and credible utilities of the claimed invention, thereby enabling the skilled artisan to use the claimed polynucleotides. Since the specification

teaches how to use the claimed polynucleotides with only routine experimentation, and the specification describes specific and immediate utilities for the claimed invention, Applicants submit that the full scope of the claims is enabled. Accordingly, it is respectfully requested that the Examiner's rejection of the claims under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

II. Rejections Under 35 U.S.C. § 112, First Paragraph

A. Written Description

The Examiner has rejected claims 166-182 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. *See* Paper No. 27, pages 4-5. In particular, the Examiner contends that:

> The specification does not contain any disclosure of the function of all DNA sequences that comprise at least 30 or 50 nucleotides of SEQ ID NO:1. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only a single species of the claimed genus which is insufficient to put on of skill in the art in possession of the attributes and features of all species within the claimed genus.

Applicants respectfully disagree and traverse this rejection.

As the Examiner noted in the Office Action, the test for the written description requirement is whether one skilled in the art could reasonably conclude that the inventor has possession of the claimed invention in the specification as filed. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991); M.P.E.P. § 2163.02; *see also Union Oil Co. v. Atlantic Richfield Co.*, 208 F.3d 989, 54 U.S.P.Q.2d

1227 (Fed. Cir. 2000); M.P.E.P. § 2163.02 ("The subject matter of the claim need not be described literally (i.e., using the same terms or in haec verba) in order for the disclosure to satisfy the description requirement.").

In an analysis of written description under 35 U.S.C. § 112, first paragraph, the Examiner bears the initial burden of presenting a *prima facie* case of unpatentability. This burden is only discharged if the Examiner can present evidence or reasons why one skilled in the art would not reasonably conclude that Applicants possessed the subject matter as of the priority date of the present application. *See In re Wertheim*, 541 F.2d 257, 262, 191 U.S.P.Q.2d 90, 96 (C.C.P.A. 1976); M.P.E.P. § 2163.04. In the instant case, the Examiner has not met this burden.

Preliminarily, Applicants note that the Examiner appears to be asserting that some functional characteristic of the claimed polynucleotides beyond the sequence disclosed in the specification is required to satisfy the written description requirement. *See* Paper No. 27, page 5. Applicants respectfully submit that since no such functional characteristic is claimed in the instant claims, then none is required to be present in order to fully describe the claimed polynucleotides. Based on the description in the specification, one of skill in the art could readily envision and identify by specific nucleotide sequence the individual polynucleotides described in the claims, and distinguish these polynucleotides from other polynucleotides that do not fit this description. Nothing more than what is described in the specification would be required. Accordingly, one skilled in the art would reasonably conclude that Applicants had possession of the polynucleotides encompassed by the rejected claims in the present application as filed.

Moreover, it cannot be questioned that the specification describes SEQ ID NO:1, yet the Examiner includes claims 171-172 in the instant rejection. Applicants respectfully

request the Examiner to clarify why claims directed to SEQ ID NO:1 and its complement in their entirety are not sufficiently described under 35 U.S.C. § 112, first paragraph.

Applicants recognize that the Examiner is in part relying on language regarding a "representative number" of a claimed genus set forth in the Guidelines for Examination of Patent Applications Under the 35 U.S.C. § 112, ¶ 1 "Written Description" Requirement ("Guidelines") when reciting the procedures followed in analyzing whether the description requirement for each of the claims at issue is satisfied. However, even assuming, *arguendo*, that the Guidelines comport with the law, the Guidelines also define a "representative number" as "an inverse function of the skill and knowledge of the art." (*See* Guidelines at page 1106). Applicants note that the level of skill in the art on the priority date of the present application was very high.

Applicants have provided the skilled artisan with the DNA (SEQ ID NO:1) and polypeptide (SEQ ID NO:2) sequences of the novel t-PALP polypeptide. Applicants have also deposited a cDNA clone with the American Type Culture Collection pursuant to the Budapest Treaty. Accordingly, one skilled in the art, enlightened by the teachings of the present application, could readily envision and identify the polynucleotide sequences that comprise the specified polynucleotides.

Moreover, it is well-established that a "gene is a chemical compound, albeit a complex one". *Amgen, Inc. v. Chugai Pharmaceutical Co., LTD.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). Thus, the claims of the instant application, directed to polynucleotides comprising at least 30 or at least 50 contiguous nucleotides of the disclosed SEQ ID NO:1, to the entire SEQ ID NO:1 (claim 171), and to the complementary sequences thereto, are essentially chemical claims involving generic chemical formulas. As stated by Judge Lourie in *University of California v. Eli Lilly*, 119 F.3d 1559 (Fed. Cir. 1997), "In claims

involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass." All of the objectives met by a generic chemical formula are similarly met by the explicit description in the instant specification of a DNA sequence (*i.e.* SEQ ID NO:1) and the instant claims to polynucleotides of at least 30 or at least 50 nucleotides thereof. That is, the instant claims clearly distinguish the boundaries of the claimed genera and identify all of the members of those genera. Accordingly, one skilled in the art would reasonably conclude that Applicants had possession of the polypeptides encompassed by the rejected claims upon reading the present application as filed.

For all of the above reasons, Applicants respectfully assert that the Examiner has failed to meet the required burden in presenting evidence or reasons why those skilled in the art would not recognize the claimed invention from the disclosure. Moreover, the specification conveys with reasonable clarity that Applicants were in possession of the claimed invention. Therefore, Applicants submit that the pending claims fully meet the written description requirements of 35 U.S.C. § 112, first paragraph, and respectfully request that the Examiner's rejection of claims 166-182 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

B. Enablement

The Examiner has rejected claims 166-182 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the claimed invention. *See* Paper No. 27, pages 6-7. In particular, the Examiner asserts that "the specification, while

being enabling for a fragment consisting of at least 30 or 50 nucleotides of SEQ ID NO:1, respectively, does not reasonably provide enablement for a fragment comprising at least 30 or 50 nucleotides of SEQ ID NO:1."

Applicants respectfully disagree and traverse this rejection.

Preliminarily, Applicants disagree that the instant claims "encompass countless number of sequences with an unknown function," as asserted by the Examiner. Rather, the instant claims encompass a distinct genus of polynucleotides comprising at least 30 or at least 50 continuous polynucleotides of SEQ ID NO:1. Applicants further disagree with the Examiner's implication that a limitation is present in the claims requiring the claimed polynucleotides to encode polypeptides. *See* Paper No. 27, page 6. Applicants point out that nothing in the instant claims requires that the claimed polynucleotides encode polypeptides, and the Examiner has not provided any support for such an interpretation of the instant claims. It is improper to read a limitation into a claim from the specification. *See, e.g.,* M.P.E.P. § 2111 at 2100-36 to 37; *In re Van Geuns*, 988 F.2d 1181, 26 U.S.P.Q.2d 1057 (Fed. Cir. 1993). Applicants emphasize that the specification does enable the use of the claimed polynucleotides to encode polypeptides, including those that retain the biological activity of the t-PALP polypeptide. However, Applicants further emphasize that the instant specification describes and teaches uses of the claimed polynucleotides that do not require them to encode polypeptides, for example, as probes for detection of the t-PALP gene and as primers to amplify t-PALP polynucleotides. *See* page 12, lines 1-12 and 24-28. Thus, since the instant claims do not contain any limitation requiring the polynucleotide to encode a polypeptide, whether the claimed polynucleotides encode polypeptides or not is irrelevant, so long as the specification enables a person of

ordinary skill in the art to practice a single use of the claimed polypeptides without undue experimentation. *See, e.g.,* M.P.E.P. § 2164.01(c).

In order to make an enablement rejection, "the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention." M.P.E.P. §2164.04; *In re Wright*, 999 F.2d 1557, 1562, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993) (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). In the absence of such a showing, a patent applicant's specification disclosure which contains a teaching of how to make and use the invention must be taken as enabling. *See In re Marzocchi*, 439 F.2d. 220, 223-224, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971); M.P.E.P. §2164.04. As stated by the court:

> it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure.

In re Marzocchi, 439 F.2d. at 224, 169 U.S.P.Q. at 370 (emphasis in original); M.P.E.P. § 2164.05. The minimal requirement is for the Examiner to give reasons for the uncertainty of the enablement. *See In re Bowen,* 492 F.2d 859, 862-63, 181 U.S.P.Q. 48, 51 (C.C.P.A. 1974); M.P.E.P. § 2164.05. In order to enable the claimed invention as required by 35 U.S.C. § 112, the specification need only enable a person of ordinary skill in the art to make the claimed polypeptides and practice a single use of the claimed polynucleotides without undue experimentation. *See, e.g.,* M.P.E.P. § 2164.01(c).

Applicants respectfully submit that the Examiner has not provided sufficient evidence or a basis to question the enablement provided in the specification for the claimed polynucleotides. In particular, since the Examiner's analysis and argument

depends upon the improper limitation of the instant claims to polynucleotides encoding polypeptides, the Examiner has not shown why the skilled artisan would not be enabled to practice any use of the claimed invention. Applicants submit that the present disclosure contains a teaching of how to make and use the invention, which must be taken as enabling absent contrary evidence. *See, e.g.,* M.P.E.P. § 2164.05.

Applicants submit that in the instant application, the disclosed or otherwise known methods of making polynucleotides may be used to make and then determine, without undue experimentation, whether a given polynucleotide encompassed by the claims can be used as a probe for detection of the t-PALP gene or as a primer to amplify t-PALP polynucleotides, the enablement requirement is fully satisfied. *See In re Wands*, 8 U.S.P.Q.2d at 1404; *Ex parte Mark*, 12 U.S.P.Q.2d 1904, 1906-1907 (B.P.A.I. 1989).

Thus, Applicants assert that the Examiner has underestimated the high level of skill of the skilled artisan, and has not considered the fact that the invention could be practiced with readily available starting materials using methods that were well known in the art on the priority date of the instant application. Applicants submit that the skilled molecular biologist, enlightened by the teaching of the present specification, is more than capable of routinely using the claimed polynucleotides, and determining, for example, whether such polynucleotides can be used as probes for detection of the t-PALP gene, as primers to amplify t-PALP polynucleotides, or encode t-PALP polypeptides, as one of ordinary skill in the art would expect of the vast majority of the claimed polynucleotides. Based on the disclosure of the present specification and the knowledge of one of ordinary skill in the art at the time the application was filed, it is clear that one of ordinary skill in the art would have been able to make and use the invention commensurate with the scope of the claims.

In view of the foregoing, Applicants submit that the pending claims fully meet the enablement requirements of 35 U.S.C. § 112, first paragraph, and respectfully request that the Examiner's rejection of claims 166-182 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

III. Rejections Under 35 U.S.C. § 112, Second Paragraph

A. Claims 88, 104, 125, 146, 157, and 174

The Examiner has rejected claims 88, 104, 125, 146, 157, and 174 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. *See* Paper No. 27, page 7. In particular, the Examiner contends that "there is insufficient antecedent basis" for the term "said heterologous polynucleotide."

In response, Applicants have amended claims 88, 104, 125, 146, 157, and 174 to depend from claims 87, 103, 124, 145, 156, and 173, respectively (which each recite the term "heterologous polynucleotide"), thereby obviating the instant rejection. In view of the foregoing, Applicants submit that the pending claims fully meet the requirements of 35 U.S.C. § 112, second paragraph, and respectfully request that the instant rejection be reconsidered and withdrawn.

B. Claims 96, 112, 133, 154, 165, and 182

The Examiner has rejected claims 96, 112, 133, 154, 165, and 182 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. *See* Paper No. 27, page 7. In particular, the Examiner contends that the claims "are unclear

because they are drawn to a method for producing a protein by culturing a host cell under conditions suitable to produce a polypeptide."

In response, although Applicants respectfully disagree with this prior rejection and assert that the previously pending claims were clear, Applicants have amended claims 96, 112, 133, 154, 165, and 182 to recite a method for producing a polypeptide, thereby obviating the instant rejection. In view of the foregoing, Applicants submit that the pending claims fully meet the requirements of 35 U.S.C. § 112, second paragraph, and respectfully request that the instant rejection be reconsidered and withdrawn.

C. Claims 114-123 and 135-144

The Examiner has rejected claims 114-123 and 135-144 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. *See* Paper No. 27, pages 7-8 . In particular, the Examiner contends that "[i]t is unclear whether claims 114-123 and 135-144 are encompassing one 'first polynucleotide' or two of the same."

In response, although Applicants respectfully disagree with this prior rejection and assert that the previously pending claims were clear, Applicants have amended claims 114-123 and 135-144 to remove the term "which further comprises," thereby obviating the instant rejection. In view of the foregoing, Applicants submit that the pending claims fully meet the requirements of 35 U.S.C. § 112, second paragraph, and respectfully request that the instant rejection be reconsidered and withdrawn.

Conclusion

In view of the foregoing remarks, Applicants believe that this application is now in condition for allowance, and an early notice to that effect is urged. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicant would expedite the examination of this application.

Finally, if there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136, such an extension is requested and the appropriate fee should also be charged to our Deposit Account.

Respectfully submitted,

Dated: January 23, 2002

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Enclosures